

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	8423	bmp or (bone adj morphogenetic adj protein)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:29
L2	228	l1 same (met or methionine or trp or tryptophan\$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:29
L3	72	l1 same (met or methionine or trp or tryptophan\$) same (substitut\$ or convert\$ or replac\$ or modify\$ or modifi\$)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:37
L4	303	l1 with antagonist\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:37
L5	6	l3 and l4	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:38
L6	497	l1 same (receptor with binding)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:40
L7	40	l2 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:39
L8	89	l1 same (receptor with binding with (domain or region or site))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:41
L9	3	l8 and l3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:42
L10	13	l1 same (receptor adj binding adj (site or domain or region))	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:43
L11	1	l10 and l2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:44
L12	0	allylsulphenyl\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:44

L13	469	allylsulph\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:45
L14	0	l13 and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:45
L15	16569	carboxymethylat\$ adn l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:45
L16	86	carboxymethylat\$ and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:45
L17	1	carboxymethylat\$ same l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:46
L18	835	(trp or tryptophan\$ or met or methionine) with alkylat\$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:47
L19	10	l18 and l1	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:48
L20	76	l1 same calcification	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:48
L21	976	l1.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:48
L22	9	l20 and l21	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:49
L23	260	calcification.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:49
L24	18	l1 and l23	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/01/27 13:49

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L9 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:719332 CAPLUS

DOCUMENT NUMBER: 139:219381

TITLE: Coupling proteins to a modified polysaccharide, especially oxidized hydroxyethyl starch for use as drugs

INVENTOR(S): Hemberger, Juergen; Orlando, Michele

PATENT ASSIGNEE(S): Biotechnologie - Gesellschaft Mittelhessen MbH, Germany

SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003074087	A1	20030912	WO 2003-EP2083	20030228
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
DE 10209821	A1	20030925	DE 2002-10209821	20020306
EP 1480682	A1	20041201	EP 2003-743359	20030228
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
PRIORITY APPLN. INFO.:			DE 2002-10209821	A 20020306
			WO 2003-EP2083	W 20030228

AB The invention relates to a method for coupling proteins to a starch-derived modified polysaccharide. The binding interaction between the modified polysaccharide and the protein is based on a covalent bond which is the result of a coupling reaction between the terminal aldehyde group or a functional group of the modified polysaccharide mol. resulting from the chemical reaction of this aldehyde group and a functional group of the protein which reacts with the aldehyde group or with the resulting functional group of the polysaccharide mol. The bond directly resulting from the coupling reaction can be optionally modified by a further reaction to the aforementioned covalent bond. The invention further relates to pharmaceutical compns. that comprise conjugates formed in this coupling process and to the use of said conjugates and compns. for the prophylaxis or therapy of the human or animal body. Thus high (130 kD) and low mol. weight (10 kD) hydroxyethyl starch was selectively oxidized and coupled to various proteins, e.g. human serum albumin, myoglobin, superoxide dismutase, streptokinase, asparaginase.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:835714 CAPLUS

DOCUMENT NUMBER: 139:305890

TITLE: Mutations in **bone morphogenetic** protein receptor 1B cause brachydactyly type A2

AUTHOR(S): Lehmann, Katarina; Seemann, Petra; Stricker, Sigmar;

Sammar, Marai; Meyer, Birgit; Suering, Katrin;
 Majewski, Frank; Tinschert, Sigrid; Grzeschik,
 Karl-Heinz; Mueller, Dietmar; Knaus, Petra; Nuernberg,
 Peter; Mundlos, Stefan
 CORPORATE SOURCE: Institut fuer Medizinische Genetik,
 Humboldt-Universitaet, Charite, Berlin, 13353, Germany
 SOURCE: Proceedings of the National Academy of Sciences of the
 United States of America (2003), 100(21), 12277-12282
 CODEN: PNASA6; ISSN: 0027-8424
 PUBLISHER: National Academy of Sciences
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Brachydactyly (BD) type A2 is an autosomal dominant hand malformation characterized by shortening and lateral deviation of the index fingers and, to a variable degree, shortening and deviation of the first and second toes. We performed linkage anal. in two unrelated German families and mapped a locus for BD type A2 to 4q21-q25. This interval includes the gene **bone morphogenetic** protein receptor 1B (BMPR1B), a type I transmembrane serine-threonine kinase. In one family, we identified a T599 → A mutation changing an isoleucine into a lysine residue (1200K) within the glycine/serine (GS) domain of BMPR1B, a region involved in phosphorylation of the receptor. In the other family we identified a C1456 → T mutation leading to an arginine-to-tryptophan amino acid change (R486W) in a highly conserved region C-terminal of the BMPR1B kinase domain. An in vitro kinase assay showed that the 1200K mutation is kinase-deficient, whereas the R486W mutation has normal kinase activity, indicating a different pathogenic mechanism. Functional analyses with a micromass culture system revealed a strong inhibition of chondrogenesis by both mutant receptors. Overexpression of mutant chBmpR1b in vivo in chick embryos by using a retroviral system resulted either in a BD phenotype with shortening and/or missing phalanges similar to the human phenotype or in severe hypoplasia of the entire limb. These findings imply that both mutations identified in human BMPR1B affect cartilage formation in a dominant-neg. manner.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 6 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2002:696621 SCISEARCH
 THE GENUINE ARTICLE: 582CJ
 TITLE: Novel anaerobic process for the recovery of methane and compost from food waste
 AUTHOR: Han S K (Reprint); Shin H S; Song Y C; Lee C Y; Kim S H
 CORPORATE SOURCE: Korea Adv Inst Sci & Technol, Dept Civil Engrn, Yusong Ku, 373-1 Kusong Dong, Taejon 305701, South Korea (Reprint); Korea Adv Inst Sci & Technol, Dept Civil Engrn, Yusong Ku, Taejon 305701, South Korea; Korea Maritime Univ, Dept Environm Engrn, Youngdo Ku, Pusan 606791, South Korea; Samsung Corp, R&D Team, Inst Technol, Engrn & Construct Grp, Yongin 449900, Kyunggi Do, South Korea
 COUNTRY OF AUTHOR: South Korea
 SOURCE: WATER SCIENCE AND TECHNOLOGY, (JUL 2002) Vol. 45, No. 10, pp. 313-319.
 Publisher: I W A PUBLISHING, ALLIANCE HOUSE, 12 CAXTON ST, LONDON SW1H0QS, ENGLAND.
 ISSN: 0273-1223.
 DOCUMENT TYPE: Article; Journal
 LANGUAGE: English
 REFERENCE COUNT: 8

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Multi-step sequential batch two-phase anaerobic composting (MUSTAC)

process was used to recover methane and composted material from food waste. The MUSTAC process consists of five leaching beds for hydrolysis, acidification and post-treatment, and an upflow anaerobic sludge blanket (UASB) reactor for methane recovery. This process involves the combined methods of sequential batch operation and two-phase anaerobic digestion for simple operation and high efficiency. Rumen microorganisms are inoculated due to their enhanced cellulolytic activity. Each leaching bed is operated in a sequential batch mode. Five leaching beds are operated in a multi-step Mode with a two-day interval between degradation stages. Acidified products in the leachate from the leaching beds are **converted** to methane in the UASB reactor. The MUSTAC process demonstrated that it was capable of removing 84.9% of volatile solids (VS) and **converting** 85.6% of biochemical methane potential (BMP) into methane at 10.9kg VS/m³-d in 10 days. Methane gas production rate was 2.31 m³/m³-d. The output from the post-treatment of residues in the same leaching bed without troublesome moving met the Korean regulation on compost, indicating that it could be used for soil amendment.

L9 ANSWER 4 OF 6 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation. on STN

ACCESSION NUMBER: 2001:428840 SCISEARCH

THE GENUINE ARTICLE: 435FJ

TITLE: Follistatin: Essential role for the N-terminal domain in activin binding and neutralization

AUTHOR: Sidis Y; Schneyer A L; Sluss P M; Johnson L N; Keutmann H T (Reprint)

CORPORATE SOURCE: Massachusetts Gen Hosp, Endocrine Unit, Wellman 501, Boston, MA 02114 USA (Reprint); Massachusetts Gen Hosp, Endocrine Unit, Boston, MA 02114 USA; Massachusetts Gen Hosp, Reprod Endocrine Unit, Boston, MA 02114 USA; Massachusetts Gen Hosp, Natl Ctr Infertil Res, Boston, MA 02114 USA; Harvard Univ, Sch Med, Boston, MA 02114 USA

COUNTRY OF AUTHOR: USA

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (25 MAY 2001) Vol. 276, No. 21, pp. 17718-17726.

Publisher: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814 USA.

ISSN: 0021-9258.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 50

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Follistatin is recognized to be an important regulator of cellular differentiation and secretion through its potent ability to bind and bionutralize activin with which it is colocalized in many tissue systems. The 288-residue follistatin molecule is comprised of a 63-residue N-terminal segment followed by three repeating 10-cysteine "follistatin domains" also represented in several extracellular matrix proteins. We have used chemical modifications and mutational analyses to define structural requirements for follistatin bioactivity that previously have not been investigated systematically. Mutant follistatins were stably expressed from Chinese hamster ovary cell cultures and assayed for activin binding in a solid-phase competition assay. Biological activities were determined by inhibition of activin-mediated transcriptional activity and by suppression of follicle-stimulating hormone secretion by cultured anterior pituitary cells. Deletion of the entire N-terminal domain, disruption of N-terminal disulfides, and deletion of the first two residues each reduced activin binding to <5 % of expressed wild-type follistatin and abolished the ability of the respective mutants to suppress activin-mediated responses in both bioassay systems. Hence, the three follistatin domains inherently lack the ability to bind or

neutralize activin. Activin binding was impaired after oxidation of at least one **tryptophan**, at position 4, in FS-288, Mutation of **Trp** to Ala or Asp at either positions 4 or 36 eliminated activin binding and bioactivity, Mutation of a third hydrophobic residue, Phe-52, reduced binding to 20% whereas **substitutions** for the individual Lys and Arg residues in the N-terminal region were tolerated. These results establish that hydrophobic residues within the N-terminal domain constitute essential activin-binding determinants in the follistatin molecule. The correlation among the effects of mutation on activin binding, activin transcriptional responses, and follicle-stimulating hormone secretion substantiates the concept that, at least in the pituitary, the biological activity of follistatin is attributable to its ability to bind and bionutralize activin.

L9 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:260344 CAPLUS

DOCUMENT NUMBER: 132:289232

TITLE: **Bone morphogenetic protein**
antagonist based on the mature protein

INVENTOR(S): Katsuura, Mieko; Kimura, Michio

PATENT ASSIGNEE(S): Hoechst Marion Roussel, Fr.

SOURCE: PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021998	A1	20000420	WO 1999-IB1621	19991004
W:			AE, AL, AU, BA, BB, BG, BR, CA, CN, CR, CU, CZ, DM, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, TZ, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
RW:			GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG	
JP 2000119192	A2	20000425	JP 1998-288103	19981009
CA 2345201	AA	20000420	CA 1999-2345201	19991004
AU 9957560	A1	20000501	AU 1999-57560	19991004
EP 1117689	A1	20010725	EP 1999-944750	19991004
R:			AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO	
JP 2002527453	T2	20020827	JP 2000-575900	19991004
PRIORITY APPLN. INFO.:			JP 1998-288103	A 19981009
			WO 1999-IB1621	W 19991004

AB The purpose is to provide a mature protein having an antagonistic activity against **bone morphogenetic** proteins. The mature protein having an antagonistic activity against **bone morphogenetic** proteins is obtained by **converting** at least one residue among **methionine** residues or **tryptophane** residues existing in the amino acid sequence of mature human **MP52** to a hydrophilic residue by chemical modification, or **replacing** said residues with a hydrophilic amino acid residue or a polar amino acid residue. The chemical modification for said methionine residue is performed by an oxidization reaction or an alkylation reaction. The chemical modification for said tryptophane residue is performed by an allylsulfonylation reaction. Or a mature protein having an antagonistic activity against **bone morphogenetic** proteins is obtained by **converting** at least one residue of **tryptophane** residues existing in the amino acid sequences of

mature human BMP-2 , mature human BMP-4 , and mature human BMP-7 to a hydrophilic residue by chemical modification, or replacing said residues with a hydrophilic amino acid residue or a polar amino acid residue. The BMP antagonists are used for therapy or prevention of ectopic ossification or metabolic diseases with calcification.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 1
 ACCESSION NUMBER: 91084512 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 2261483
 TITLE: Fluorescent oligopeptide substrates for kinetic characterization of the specificity of Astacus protease.
 AUTHOR: Stocker W; Ng M; Auld D S
 CORPORATE SOURCE: Department of Physiology, University of Heidelberg, FRG.
 SOURCE: Biochemistry, (1990 Nov 13) 29 (45) 10418-25.
 Journal code: 0370623. ISSN: 0006-2960.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199102
 ENTRY DATE: Entered STN: 19910322
 Last Updated on STN: 20000303
 Entered Medline: 19910207

AB The design of fluorescent N-dansylated oligopeptides based on the tubulin cleavage pattern by Astacus protease yields substrates that are turned over up to 10(5) times faster than those presently available. On the basis of this study, an optimal substrate for Astacus protease contains seven or more amino acids and minimally requires at least five amino acids. Direct examination of the formation and breakdown of the ES complex shows its formation occurs within milliseconds at 25 degrees C. The best heptapeptide substrate, Dns-Pro-Lys-Arg-Ala-Pro-Trp-Val, is cleaved only between the Arg-Ala (P1-P1') bond with kinetic parameters $k_{cat} = 380 \text{ s}^{-1}$ and $K_m = 3.7 \times 10^{-4} \text{ M}$. The presence of Lys or Arg in the P1 and P2 positions yields high-turnover substrates. In the P3 position, the enzyme prefers Pro greater than Val greater than Leu greater than Ala greater than Gly, following the same order of preference seen in the tubulin cleavage pattern. Substitution of Leu for Ala in P1' and of Ser for Pro in P2' decreases activity by 10(5)- and 10(2)-fold, respectively. In position P3', substitution of Trp for Leu leaves the activity unaltered. However, introduction of the Trp fluorophore greatly enhances the sensitivity of the assay due to a 10-fold increase in indole fluorescence for cleavage of any peptide bond between the tryptophan and the dansyl group. Such an energy-transfer-based assay should have widespread use for detection of neutral proteases. (ABSTRACT TRUNCATED AT 250 WORDS)

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(FILE 'HOME' ENTERED AT 12:38:40 ON 27 JAN 2005)

FILE 'MEDLINE, CAPLUS, SCISEARCH, BIOSIS' ENTERED AT 12:38:54 ON 27 JAN 2005

L1 27217 S (BMP OR (BONE(W)MORPHOGENETIC) OR MP52)
 L2 3 S L1(P) ((MET OR METHIONINE OR TRYPTOPHAN OR TRYPTOPHANE) (S) (CON
 L3 3 DUP REM L2 (0 DUPLICATES REMOVED)
 L4 34939 S (MET OR TRP OR TRYPTOPHAN? OR METHIONIN?) (S) (CONVERT? OR SUBS
 L5 230751 S RECEPTOR AND BIND? AND (DOMAIN OR REGION OR SITE)
 L6 650 S L1(P)L5

L7	0 S L6 AND L4
L8	8 S L1 AND L4
L9	6 DUP REM L8 (2 DUPLICATES REMOVED)
L10	0 S L9 AND L5